

AMENDMENTS TO THE CLAIMSAmendment to the Claims:

Please amend the claims as follows:

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method of identifying a function of a polypeptide-encoding sequence of interest endogenously expressed by a cell type using high throughput detection, comprising:

a) providing at least a first and a second pseudotyped lentiviral vector, each comprising at least a part of the polypeptide-encoding sequence of interest or a complementary sequence thereof, wherein the polypeptide-encoding sequence of interest is a known or unidentified gene sequence, and wherein the first lentiviral vector is designed to express little or no vector borne sequence other than the at least a part of the polypeptide-encoding sequence of interest, and

wherein the first lentiviral vector is designed to overexpress only the endogenously expressed polypeptide encoding sequence of interest

b) and the providing a second pseudotyped lentiviral vector, is designed to inhibit or terminate expression of the endogenously expressed polypeptide-encoding sequence of interest comprising an inhibitory or termination sequence, wherein the inhibitory or termination sequence can inhibit, terminate, or underexpress the endogenously expressed polypeptide-encoding sequence of interest, and

wherein the second lentiviral vector is designed to express little or no vector borne sequence other than the inhibitory or termination sequence,

and the at least first and second pseudotyped lentiviral vectors are designed to express no viral protein encoding sequences and each express sequences comprising the polypeptide-encoding sequence of interest in either a sense or an antisense orientation;

[[b]] c) providing a first and a second population of the cell type, and transducing the first lentiviral vector in the first cell population and transducing the second lentiviral vector in the second cell population;

[[c]] d) overexpressing all or part of [[said]] the polypeptide-encoding sequence of interest in the first cell population of said cell type and inhibiting, [[or]] terminating, or underexpressing expression of said the polypeptide-encoding sequence of interest in the second cell population of said cell type;

[[d]] e) high throughput detecting at least one change in one or more endogenous cellular factors in [[said]] the first and second cell populations [[and]] by comparing the effect on the cell of overexpression of the polypeptide-encoding sequence of interest with the effect on the cell of inhibition, or termination, or underexpression of expression of the polypeptide-encoding sequence of interest; and

[[e]] f) identifying a function of [[said]] the polypeptide-encoding sequence of interest based on the detected and compared effect on the cell of overexpression and inhibition, or termination, of expression or underexpression of [[said]] the polypeptide-encoding sequence of interest on one or more cellular factors.

Claim 2 (currently amended): The method of claim 1, wherein [[said]] the at least one change is an increase and/or decrease in the expression of [[said]] the endogenous cellular factor[[s]].

Claim 3 (currently amended): The method of claim 1, wherein [[said]] the at least one change is in a post-translational modification of [[said]] the endogenous cellular factor[[s]].

Claim 4 (currently amended): The method of claim 3, wherein [[said]] the post-translational modification comprises a phosphorylation or glycosylation of [[said]] the cellular factor[[s]].

Claim 5 (currently amended): The method of claim 1, wherein [[said]] the at least one change is in an activity of [[said]] the cellular factor[[s]].

Claim 6 (currently amended): The method of claim 1, wherein [[said]] the first and/or second pseudotyped lentiviral vector is a conditionally replicating pseudotyped lentiviral vector.

Claim 7 (currently amended): The method of claim 1, wherein [[said]] the inhibiting expression of said polypeptide-encoding sequence in a second population is by use of a pseudotyped lentiviral vector capable of expressing inhibitory or termination sequence comprises all or part of [[said]] the polypeptide-encoding sequence of interest in an antisense orientation.

Claim 8 (currently amended): The method of claim 1, wherein [[said]] the inhibiting or terminating expression of said polypeptide-encoding sequence in a second population is by use of a pseudotyped lentiviral vector capable of expressing inhibitory or termination sequence comprises a sequence encoding for one or more ribozymes against [[said]] the polypeptide-encoding sequence of interest.

Claim 9 (currently amended): The method of claim 1, wherein [[said]] the inhibiting or terminating expression of said polypeptide-encoding sequence in a second population is by the generation of post transcriptional gene silencing (PTGS) inhibitory or termination sequence comprises a sequence encoding a double stranded RNA against [[said]] the polypeptide-encoding sequence of interest.

Claim 10 (currently amended): The method of claim 1, wherein [[said]] the cell type is a primary cell.

Claims 11 to 13 (canceled)

Claim 14 (currently amended): The method of claim 1, wherein [[said]] the polypeptide-encoding sequence of interest encodes a product which modulates expression of [[said]] the one or more cellular factors by binding to nucleic acids encoding, or regulating the expression of, [[said]] the one or more cellular factors.

Claim 15 (currently amended): The method of claim [[12]] 14, wherein [[said]] the polypeptide-encoding sequence of interest encodes a transcriptional activator.

Claim 16 (currently amended): The method of claim [[12]] 14, wherein [[said]] the polypeptide-encoding sequence of interest encodes a transcriptional repressor.

Claim 17 (currently amended): The method of claim 1, wherein [[said]] the polypeptide-encoding sequence of interest is a human sequence.

Claim 18 (currently amended): The method of claim 1, wherein [[said]] the cell type is a human, a plant or a microorganism cell type.

Claim 19 (currently amended): A method of altering the expression of one or more cellular factors in a cell comprising overexpressing or inhibiting, terminating, or underexpressing the expression of a gene sequence for which a function was identified by the method of claim 1.

Claim 20 (currently amended): A method of altering the phenotype of a cell comprising overexpressing or inhibiting, terminating, or underexpressing a gene sequence for which a function was identified by the method of claim 1.

Claim 21 (currently amended): A method of identifying a function of a gene sequence of interest in a cell heterologous to the cellular source of [[said]] the gene sequence of interest using high throughput detection, comprising:

a) providing at least a first and a second pseudotyped lentiviral vector, each comprising at least a part of the gene sequence of interest or a complementary sequence thereof, wherein the gene sequence of interest is a known gene sequence, and wherein the pseudotyped lentiviral vector is designed to express little or no vector borne sequence other than the at least a part of the gene sequence of interest, and

wherein the first lentiviral vector is designed to overexpress the expressed gene sequence of interest and the second lentiviral vector is designed to underexpress or terminate the expressed gene sequence of interest, and overexpression and underexpression or termination is relative to the level of expression of the gene sequence in [[the]] a cell from which the gene sequence was derived,

and the at least first and second pseudotyped lentiviral vectors are designed to express no viral protein encoding sequences and each express sequences comprising the gene sequence of interest in either a sense or an antisense orientation;

(b) providing a ~~first and a second~~ population of the cell, and transducing the ~~first~~ lentiviral vector in ~~a first~~ the cell population ~~and transducing the second lentiviral vector in a second cell population;~~

(c) ~~overexpressing all or part of [[said]] the gene sequence of interest in the first cell population of said cell and inhibiting or terminating expression of said sequence in a second population of said cell type;~~

(d) high throughput detecting at least one change in one or more cellular factors in ~~[[said]] the cell population when compared to the expression of the gene sequence of interest in the cell from which the gene sequence was derived first and second populations and comparing the effect on the cell of overexpression of the gene sequence with the effect on the cell of inhibition or termination of expression of the gene sequence; and~~

(e) identifying a function of ~~[[said]] the gene sequence of interest based on the detected and compared effect on the cell of overexpression of the gene sequence of interest and inhibition or termination of expression of said one or more cellular factors expression of the gene sequence of interest in the cell from which the gene sequence was derived, on one or more cellular factors.~~

Claim 22 (currently amended): A method of detecting, using high throughput detection, a change in one or more cellular factors in a cell due to the ~~overexpression [[or]] and inhibition, termination, or underexpression~~ of a gene sequence of interest in ~~[[said]] the~~ cell, comprising:

a) providing at least a first and a second pseudotyped lentiviral vector, each comprising a part of the gene sequence of interest or a complementary sequence thereof;

wherein the first lentiviral vector is designed to overexpress the expressed gene sequence of interest and the second lentiviral vector is designed to underexpress or terminate the expressed gene sequence of interest, and overexpression and underexpression or termination is relative to the level of expression of the gene sequence in the cell from which the gene sequence was derived;

and the at least first and second pseudotyped lentiviral vectors are designed to express no viral protein encoding sequences and each express sequences comprising the gene sequence of interest in either a sense or an antisense orientation;

(b) providing a first and a second population of the cell, and transducing the first lentiviral vector in a first cell population and transducing the second lentiviral vector in a second cell population;

(c) overexpressing all or part of said gene sequence in the first population of said cell type and inhibiting expression of said gene sequence in a second population of said cell type; and

(d) high throughput detecting at least one change in one or more cellular factors in said first and second populations by comparing the effect on the cell of overexpression of the gene sequence with the effect on the cell of inhibition or termination of expression of the gene sequence

a) providing a first pseudotyped lentiviral vector, comprising at least a part of the gene sequence of interest, wherein the gene sequence of interest is a known or unidentified gene sequence, and wherein the first lentiviral vector is designed to express little or no vector borne sequence other than the at least a part of the gene sequence of interest, and

b) providing a second pseudotyped lentiviral vector, comprising an inhibitory or termination sequence, wherein the inhibitory or termination sequence can inhibit, terminate, or underexpress the gene sequence of interest, and

wherein the second lentiviral vector is designed to express little or no vector borne sequence other than the inhibitory or termination sequence,

c) providing a first and a second population of the cell type, and transducing the first lentiviral vector in the first cell population and transducing the second lentiviral vector in the second cell population;

d) expressing all or part of the gene sequence of interest in the first cell population and inhibiting, terminating, or underexpressing the gene sequence of interest in the second cell population; and

e) high throughput detecting at least one change in one or more endogenous cellular factors in the first and second cell populations by comparing the effect on the cell of expression of the gene sequence of interest with the effect on the cell of inhibition, termination, or underexpression of the gene sequence of interest.

Claim 23 (currently amended): The method of claim 22, further comprising a step:

[[(e)]] f identifying [[the]] a function of [[said]] the gene sequence of interest based on the detected and compared effect on the cell of overexpression and inhibition, [or] termination, or underexpression of expression of [[said]] the gene sequence of interest on one or more cellular factors.

Claim 24 (currently amended): The method of claim 23, further comprising a step:

[[(f)]] g altering the expression of [[said]] the one or more cellular factors in a third population of [[said]] the cell type cell by overexpressing or inhibiting or terminating the expression of [[said]] the gene sequence of interest for which a function was identified in step [[(e)]] f.

Claim 25 (currently amended): The method of claim 23, further comprising a step:

[[(f)]] g altering the phenotype of a third population of [[said]] the cell type by overexpressing or inhibiting, terminating, or underexpressing the expression of said gene sequence of interest for which a function was identified in step [[(e)]] f.

Claim 26 (currently amended): The method of claim 22, wherein [[said]] the cell is heterologous to the cellular source of [[said]] the gene sequence of interest, and overexpression and underexpression or terminate termination is relative to the level of expression of the gene sequence of interest in [[the]] a cell from which the gene sequence of interest was derived.

Claim 27 (currently amended): The method of claim 22, wherein [[said]] the cellular factor comprises a cellular gene product or a metabolite.

Claim 28 (currently amended): The method of claim 27, wherein [[said]] the cellular gene product comprises a protein or RNA.

Claim 29 (currently amended): The method of claim 27, wherein [[said]] the metabolite comprises a sugar or a lipid.

Claim 30 (currently amended): The method of claim 1, wherein inhibiting, [[or]] terminating, or underexpressing expression of the polypeptide-encoding sequence of interest is mediated by post-transcriptional gene silencing (PTGS), small interfering RNA (siRNA), RNA

interference, or an antisense or a ribozyme sequence targeted against the polypeptide-encoding sequence of interest.

Claim 31 (previously presented): The method of claim 1, wherein the high throughput detecting comprises use of computerized or robot implemented systems.

Claim 32 (currently amended): The method of claim ~~[[31]] 1~~, wherein the high throughput detecting comprises use of libraries of pseudotyped lentiviral vectors and cells transduced by the pseudotyped lentiviral vectors.

Claim 33 (currently amended): The method of claim ~~[[31]] 1~~, wherein the high throughput detecting comprises use of libraries of pseudotyped lentiviral vectors and cells transduced by the pseudotyped lentiviral vectors in a multiplicity of compartments.

Claim 34 (previously presented): The method of claim 1, wherein the high throughput detecting comprises use of machine implemented microarray or macroarray technology.

Claim 35 (cancelled)

Claim 36 (previously presented): The method of claim 21, wherein the high throughput detecting comprises use of computerized or robot implemented systems.

Claim 37 (new): The method of claim 22, wherein the high throughput detecting comprises use of computerized or robot implemented systems.

Claim 38 (new): The method of claim 1, wherein the inhibitory or termination sequence comprises a sequence encoding a short interfering (si) RNA.

Claim 39 (new): The method of claim 1, wherein the inhibitory or termination sequence comprises an antisense sequence ligated to a co-localization sequence.